REMARKS

1. Objection to Claim 1

Claim 1 was objected to due to the inclusion of "(a)" in line 2. Applicants have amended the claim as requested by the Examiner.

2. Rejection of Claims 1, 2 and 10-12 under 35 U.S.C. 112, first paragraph

Claims 1, 2 and 10-12 were rejected under 35 U.S.C. 112, first paragraph, written description as set forth in the Office Action.

a. Initially, Applicants note that they disagree with the Examiner's statement that the specification fails to describe any nucleic acid molecule comprising a nucleic acid sequence SEQ ID NO: 8 or 10 or any nucleic acid encoding SEQ ID NO:9. The specification describes the isolation, sequencing and commercialization of cDNA's encoding two different full-length TAg1 proteins (protein SEQ ID NOs. 3 and 18). Claimed nucleic acid SEQ ID NOs. 8 and 10 represent the forward and reverse strands of the 5' end of the disclosed full-length cDNA and protein SEQ ID NO:9 therefore represents the N-terminus of the disclosed full-length protein. One of the full-length variants is further characterized in the specification as containing 13 exons, the location of which are identified. Therefore, while the present claims recite partial sequences, the full-length sequences are disclosed and the claims to the partials should be accorded the same claim breadth as the full-length sequences, which the Applicants have the right to claim, but elected not to pursue in this application.

Accordingly, Applicants respectfully assert that the Examiner's argument that the specification describes at most nucleic acid molecules consisting of SEQ ID NOs. 8 and 10 is erroneous, see Training Example No. 8 of the Synopsis of Application of Written Description

Guidelines, which was prepared by the USPTO to train Examiners how to apply the written description requirements of 35 U.S.C. 112, set out in Federal Register, Vol. 66, No. 4, pages 1099-1111.

b. With respect to the Examiner's argument that the specification does not adequately describe variants of SEQ ID NOs. 8 and 10 and further that the skilled artisan cannot envision all possible variant nucleic acid or protein sequences, Applicants respectfully traverse.

Initially, Applicants reiterate that the specification describes 2 different variants (identical except for a 3 amino insertion, see page 84, line 4 of the specification) of canine TAg1. Applicants further note that Claim 10 has been amended to recite nucleic acid molecules comprising SEQ ID NOs. 8 and 10, thereby removing reference to any variants and rendering the rejection moot with respect to Claim 10 and its dependents.

With respect to Claim 1, which recites hybrids of the TAg1 nucleic acid molecules described by the present invention, and claims dependent thereon, Applicants traverse in view of the claim amendments set forth above in which the hybridization conditions have been amended to recite a wash temperature which will yield hybrids at 90% stringency. Support for this amendment may be found in the specification at page 17, line 9 through page 21, line 2 and at page 40, lines 8-22. Applicants respectfully argue that the claims meet the requirements of 35 U.S.C. 112, 1st paragraph as set out in the Synopsis of Application of Written Description Guidelines, Example 9 because the present specification sets out the highly stringent hybridization conditions used to obtain nucleic and amino acid sequences of the present invention. Further, one of skill in the art would not expect substantial variations among proteins encompassed within the

scope of the claims because the hybridization conditions set forth in the claim yield structurally similar cDNAs.

c. Applicants note that new claims 24-27 also contain variations of SEQ ID NOs. 8 and 10 due to claiming nucleic acid molecules encoding SEQ ID NO:9 and variants thereof that are at least 95% identical to SEQ ID NO:9 and possess canine TAg1 activity. Applicants respectfully argue that Claims 24-27 and the specification satisfy the requirements of 35 U.S.C. 112, first paragraph and direct the Examiner to the guidance provided by Example No. 14 of the Synopsis of Application of Written Description Guidelines, which was prepared by the USPTO to train Examiners how to apply the requirements set out in Federal Register, Vol. 66, No. 4, pages 1099-1111.

Training Example 14 describes a hypothetical specification which discloses a single protein species, SEQ ID NO:3, which catalyzes the reaction of A to B. The specification contemplates, but does not exemplify, variants having the same activity. The specification further indicates that procedures for making variants are routine and provides an assay for testing such variants for activity. Based upon the foregoing, the applicant in Example 14 claims a protein having SEQ ID NO:3 and variants that are at least 95% identical to SEQ ID NO:3 and catalyze the reaction of A to B.

The USPTO analyzed the adequacy of the written description of Example 14 as follows. "The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO:3 which are capable of the specified activity. One of skill in the art would conclude that applicant

was in **possession of the necessary common attributes** possessed by the members of the genus" (emphasis added). Applicants note that the USPTO analysis correctly concludes that description of the necessary common attributes of the genus is what is required to satisfy 35 U.S.C. 112, first paragraph, and not physical possession of some arbitrary number of species exhibiting that activity. Accordingly, Applicants respectfully assert, and argue that the USPTO analysis concurs, that a single disclosed species can adequately define a genus of structurally similar molecules having the same functional property, and is thus consistent with the requirements as set forth in *Regents of the University of California v. Eli Lilly and Company*, 119 F3d 1559 at 1569, 43 USPQ2d at 1406, which calls for "recitation of a representative number of polypeptide sequences *** **or of a recitation of structural features common to the genus**" (emphasis added).

In view of the foregoing, Applicants respectfully request withdrawal of the Examiner's rejection of Claims 1, 2 and 10-12 under 35 U.S.C. 112, first paragraph.

3. Rejection of Claims 2-5 and 11 under 35 U.S.C. 112, second paragraph

Claims 2-5 and 11 were rejected under 35 U.S.C. 112, second paragraph as indefinite as set forth in the office action. In order to clarify, Applicants have amended the claims to specify "an isolated nucleic acid molecule" in each of the rejected claims as set forth above. In view of the foregoing, Applicants respectfully request withdrawal of the Examiner's rejection of Claims 2-5 and 11 under 35 U.S.C. 112, second paragraph.

4. Rejection of Claims 10 and 12 under 35 U.S.C. 102(b)

Claims 10 and 12 were rejected under 35 U.S.C. 102(b) as anticipated by Sanicola-Nadel et al. Specifically, the Examiner noted that the reference teaches 16 amino acids which are 100% identical to 16 amino acids of SEQ ID NO:9 of the present invention.

In order to expedite allowance of claims, Applicants have amended Claim 10 to recite a nucleic acid molecule encoding a protein comprising SEQ ID NO:9 and nucleic acids complementary thereto. In view of the foregoing, Applicants respectfully request withdrawal of the Examiner's rejection of Claims 10 and 12 under 35 U.S.C. 102(b).

5. Rejection of Claims 1, 3, 5, and 6 under 35 U.S.C. 102(b) and 35 U.S.C. 103(a)

Claims 1, 3, 5, and 6 were rejected under 35 U.S.C. 102(b) or in the alternative under 35 U.S.C. 103(a) over Sanicola-Nadel et al. Specifically, the Examiner argued that nucleotides 255-407 of SEQ ID NO:85 taught in the reference are 84.3% identical to SEQ ID NO:8 of the present invention. In order to expedite allowance of claims, Applicants have amended Claim 1 to recite hybridization and wash conditions which will result in about 90% stringency. Applicants argue that the reference, which discloses a rat Kidney Injury associated Molecule (KIM), neither teaches nor suggests nucleic acid molecules that are 90% identical to a canine tumor antigen of the present invention due to the vastly different sources and functions of the molecules in question. One of skill in the art would not be motivated and would not have a reasonable expectation of success in isolating nucleic acid molecules claimed by the present invention based upon the teachings of Sanicola-Nadel et al.

In view of the foregoing, Applicants respectfully request withdrawal of the Examiner's rejection of Claims 1, 3, 5, and 6 under 35 U.S.C. 102(b) and 35 U.S.C. 103(a).

6. Rejection of Claim 4 under 35 U.S.C. 103(a)

The Examiner rejected Claim 4 under 35 U.S.C. 103(a) as obvious over Sanicola-Nadel et al. in view of Lathe et al. Specifically, the Examiner applied Sanicola-Nadel et al. as set forth above and applied Lathe et al. as teaching the production of a recombinant virus comprising a

tumor specific antigen. Accordingly, the Examiner argued that one of skill in the art would have known to combine the nucleic acid molecule of Sanicola-Nadel et al. with Lathe et al. to produce a recombinant virus comprising such a nucleic acid molecule.

In view of the amendments made in response to the Examiner's rejection as set forth in section 5 above, Applicants respectfully argue that neither of the references, alone or in combination, teaches or suggests a nucleic acid molecule 90% identical to a nucleic acid molecule of the present invention. Accordingly, even if the combined teachings could be used for production of a recombinant virus with a different nucleic acid molecule, such combination does not render production of a recombinant virus comprising a nucleic acid of the present invention obvious.

In view of the foregoing, Applicants respectfully request withdrawal of the Examiner's rejection of Claim 4 under 35 U.S.C. 103(a).

In the event the Examiner has any questions regarding this application, the Examiner is invited to contact the Applicant's undersigned representative at (970)493-7272.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

Please amend Claims 1-5 and 10-11 and add Claims 24-27without prejudice or disclaimer of the subject matter thereof, as follows (Claims 6-9 and 12-15 are presented below unamended for the Examiner's convenience):

1. (Twice Amended) An isolated [nucleic acid molecule selected from the group consisting of: (a) an isolated] canine cDNA or mRNA [nucleic acid molecule] that hybridizes with a nucleic acid molecule consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO:8 and SEQ ID NO:10 under conditions comprising (i) hybridizing in a solution comprising 1X SSC in the absence of nucleic acid helix destabilizing agents, at a temperature of about 37°C and (ii) washing in a solution comprising 1X SSC in the absence of nucleic acid helix destabilizing agents, at a temperature of about 76°C [56°C].

2. (Twice Amended) The isolated nucleic acid molecule of Claim 1, said nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:8 and SEQ ID NO:10.

3. (Once Amended) A recombinant molecule comprising [a] an isolated nucleic acid molecule as set forth in Claim 1 operatively linked to a transcription control sequence.

4. (Once Amended) A recombinant virus comprising [a] an isolated nucleic acid molecule as set forth in Claim 1.

5. (Once Amended) A recombinant cell comprising [a] an isolated nucleic acid molecule as set forth in Claim 1.

6. A composition comprising an isolated nucleic acid molecule of Claim 1 and a component selected from the group consisting of an excipient, an adjuvant and a carrier.

7. A method to produce a protein encoded by an isolated nucleic acid molecule of Claim 1, said method comprising culturing a cell transformed with a nucleic acid molecule encoding said protein.

8. (Once Amended) The method of Claim 7, wherein said nucleic acid molecule encodes a protein having an amino acid sequence SEQ ID NO:9.

9. (Once Amended) The method of Claim 7, wherein said nucleic acid molecule comprises a nucleic acid sequence SEQ ID NO:8.

10. (Once Amended) An isolated nucleic acid molecule selected from the group consisting of: (a) an isolated nucleic acid molecule encoding a protein comprising an amino acid sequence SEQ ID NO:9; and (b) [an isolated nucleic acid molecule encoding a protein comprising an at least 6 consecutive amino acid portion identical in sequence to an at least 6 consecutive amino acid portion of SEQ ID NO:9; and (c)] a nucleic acid molecule complementary to a nucleic acid molecule of (a)[or (b)].

11. (Twice Amended) The isolated nucleic acid molecule of Claim 10, wherein said nucleic acid molecule encodes a protein having an amino acid sequence SEQ ID NO:9.

12. A composition comprising an isolated nucleic acid molecule of Claim 10 and a component selected from the group consisting of an excipient, an adjuvant and a carrier.

13. A method to produce a protein encoded by an isolated nucleic acid molecule of Claim 10, said method comprising culturing a cell transformed with a nucleic acid molecule encoding said protein.

14. (Once Amended) The method of Claim 13, wherein said nucleic acid molecule encodes a protein having an amino acid sequence SEQ ID NO:9.

15. (Once Amended) The method of Claim 13, wherein said nucleic acid molecule comprises a nucleic acid sequence SEQ ID NO:8.

24. (Added) An isolated nucleic acid molecule that encodes a protein having an amino acid sequence selected from the group consisting of SEQ ID NO:9 and variants thereof that are at least 95% identical to SEQ ID NO:9, wherein said variants exhibit TAg1 activity.

25. (Added) The isolated nucleic acid molecule of Claim 24, said nucleic acid molecule comprising a nucleic acid sequence SEQ ID NO:8.

26. (Added) A composition comprising an isolated nucleic acid molecule of Claim 24 and a component selected from the group consisting of an excipient, an adjuvant and a carrier.

27. (Added) A method to produce a protein encoded by an isolated nucleic acid molecule of Claim 24, said method comprising culturing a cell transformed with a nucleic acid molecule encoding said protein.

SYNOPSIS OF APPLICATION OF WRITTEN DESCRIPTION GUIDELINES

Contents

SYNOPSIS OF APPLICATION OF WRITTEN DESCRIPTION GUIDELINES

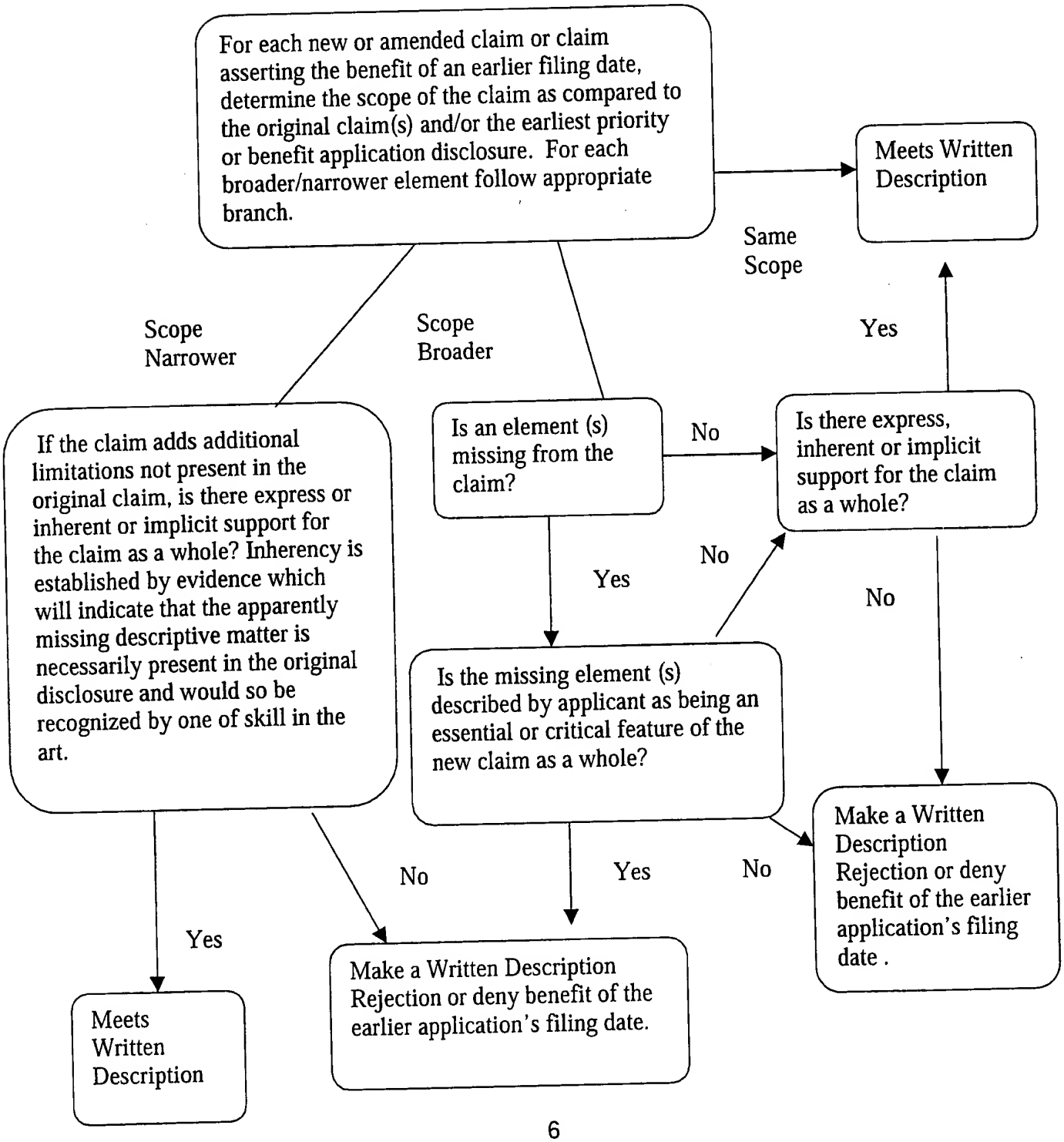
It is assumed at this point in the analysis that the specification has been reviewed and an appropriate search of the claimed subject matter has been conducted. It is also assumed that the examiner has identified which features of the claimed invention are conventional taking into account the body of existing prior art. There is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed. If the examiner determines that the application does not comply with the written description requirement, the examiner has the initial burden, after a thorough reading and evaluation of the content of the application, of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims. It should also be noted that the test for an adequate written description is separate and distinct from the test under the enablement criteria of 35 U.S.C. § 112 first paragraph. The absence of definitions or details for well-established terms or procedures should not be the basis of a rejection under 35 U.S.C. 112, para. 1, for lack of adequate written description. Limitations may not, however, be imported into the claims from the specification.

The following examples only describe how to determine whether the written description requirement of 35 U.S.C. 112, para. 1 is satisfied. Regardless of

the outcome of that determination, Office personnel must complete the patentability determination under all the relevant statutory provisions of Title 35 of the U.S. Code. Once Office personnel have concluded analysis of the claimed invention under all the statutory provisions, including 35 U.S.C. 101, 112, 102, and 103, they should review all the proposed rejections and their bases to confirm their correctness. Only then should any rejection be imposed in an Office action. The Office action should clearly communicate the findings, conclusions, and reasons which support them. When possible, the Office action should offer helpful suggestions on how to overcome rejections.

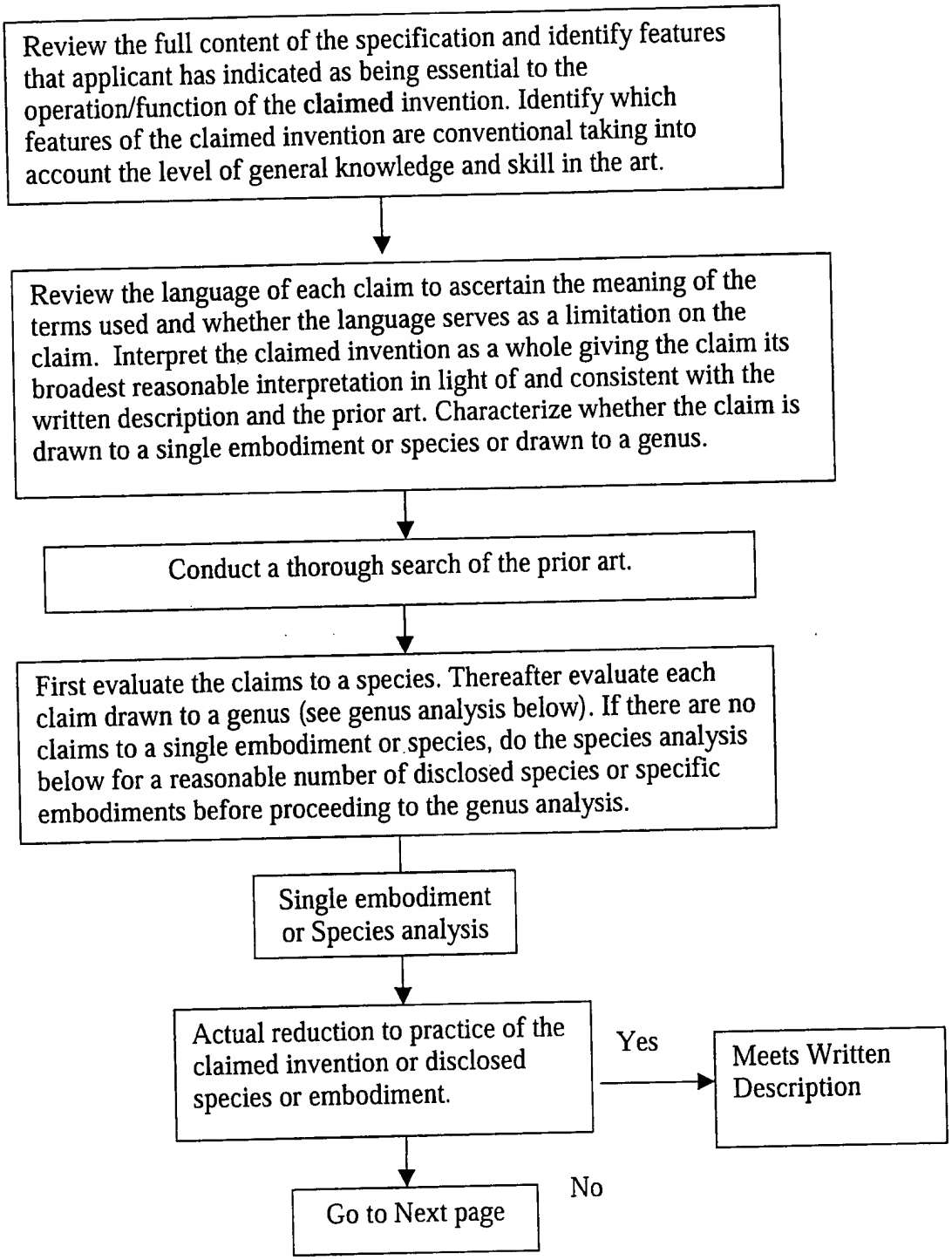
Written Description Amended or New Claims, or Claims Asserting the Benefit of an Earlier Filing Date

Decision Tree



Written Description
Original Claims

--Decision Tree--



Written Description

Original Claims

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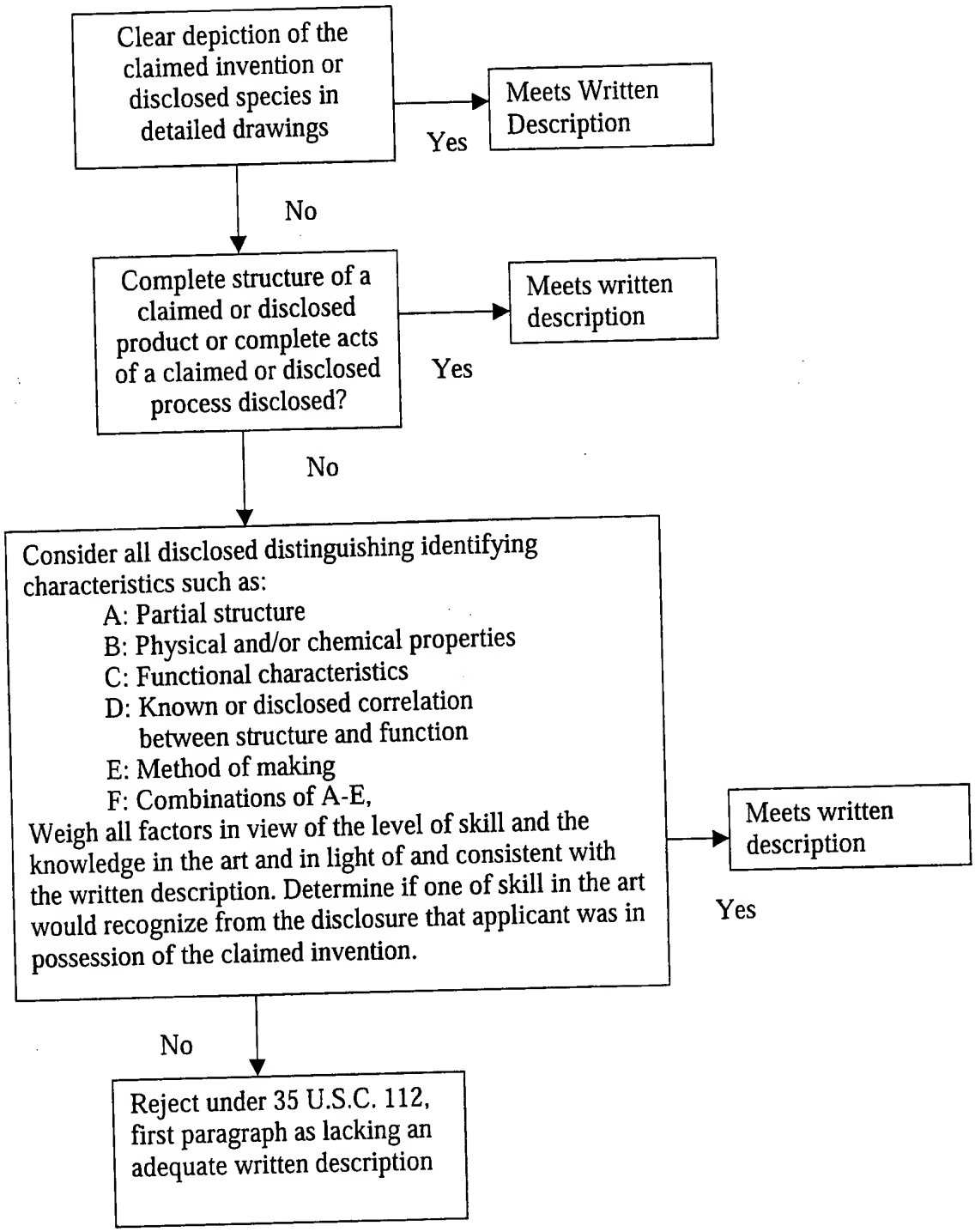

Written Description

Original Claims

Decision Tree

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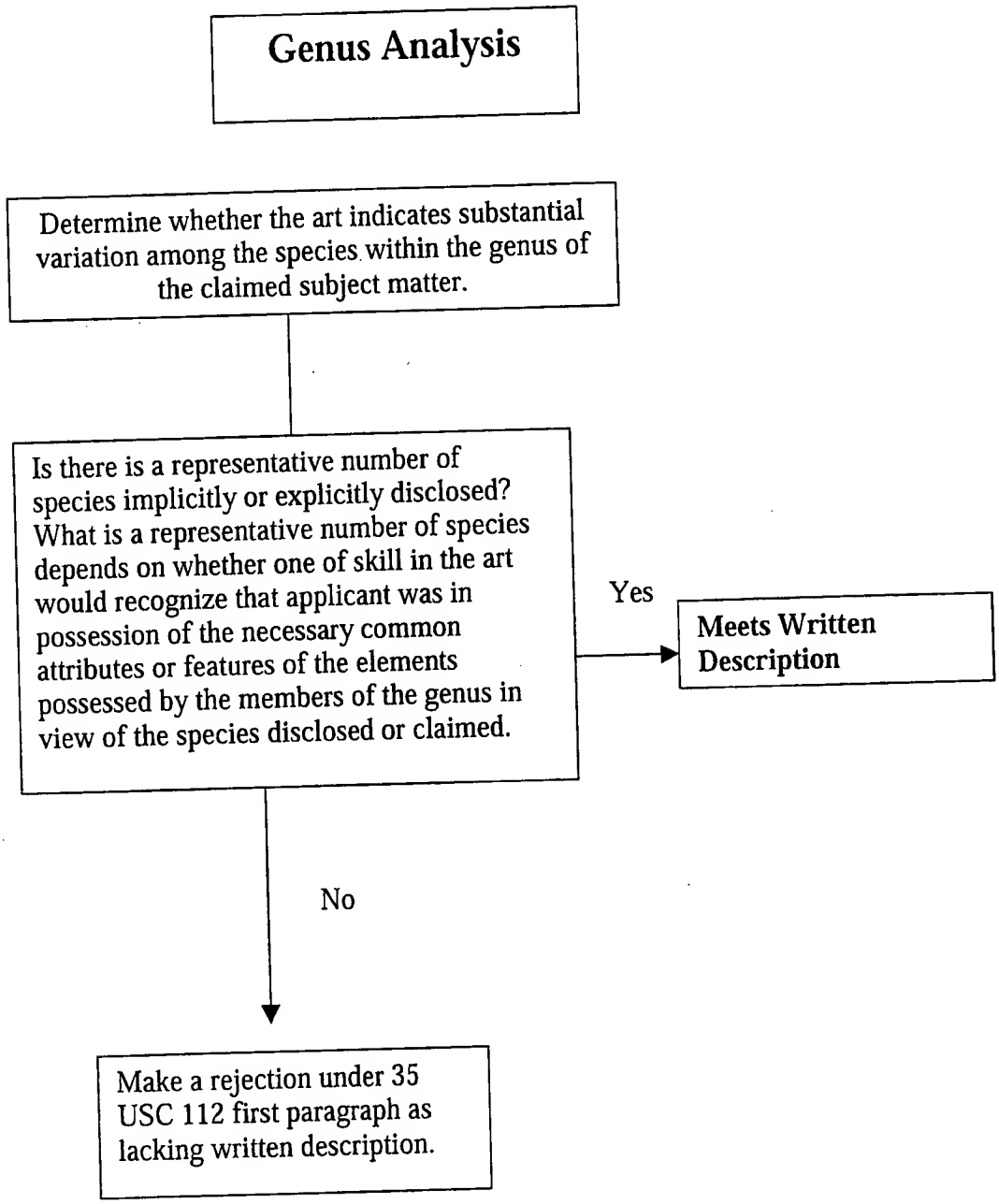

Caveat: *In situations where the specification indicates that the SEQ ID NO: is a full-length cDNA open reading frame and the claim cannot read on a gene, the claimed invention would meet the written description requirement.*

Example 8: DNA fragment Encoding a Full Open Reading Frame (ORF)

Specification: The specification discloses that a cDNA library was prepared from human kidney epithelial cells and 5000 members of this library were sequenced and open reading frames were identified. The specification discloses a Table that indicates that one member of the library having SEQ ID NO: 2 has a high level of homology to a DNA ligase. The specification teaches that this complete ORF (SEQ ID NO: 2) encodes SEQ ID NO: 3. An alignment of SEQ ID NO: 3 with known amino acid sequences of DNA ligases indicates that there is a high level of sequence conservation between the various known ligases. The overall level of sequence similarity between SEQ ID NO: 3 and the consensus sequence of the known DNA ligases that are presented in the specification reveals a similarity score of 95%. A search of the prior art confirms that SEQ ID NO: 2 has high homology to DNA ligase encoding nucleic acids and that the next highest level of homology is to alpha-actin. However, the latter homology is only 50%. Based on the sequence homologies, the specification asserts that SEQ ID NO: 2 encodes a ligase.

Claim 1: An isolated and purified nucleic acid comprising SEQ ID NO: 2.

Analysis:

A review of the full content of the specification indicates SEQ ID NO: 2 is essential to the operation and function of the claimed invention. The specification indicates that SEQ ID NO: 2 encodes a protein that would be expected to act as a DNA ligase.

A review of the language of the claim indicates that the claim is drawn to a genus, i.e., any nucleic acid that minimally contains SEQ ID NO: 2. The claim is drawn to a nucleic acid comprising a full open reading frame. The claimed nucleic acid does not read on a genomic sequence because full-length mammalian cDNAs would not be expected to contain introns or transcriptional regulatory elements such as promoters that are found in genomic DNA. The claim reads on the claimed ORF in any construct or with additional nucleic acid residues placed at either end of the ORF.

The search indicates that SEQ ID NO: 2 is a novel and unobvious sequence.

There is a single species explicitly disclosed (a molecule consisting of SEQ ID NO: 2 that is within the scope of the claimed genus).

There is actual reduction to practice of the disclosed species.

One of skill in the art can readily envisage nucleic acid sequences which include SEQ ID NO: 2 because e.g. SEQ ID NO: 2 can be readily embedded in known vectors. Although there may be substantial variability among the species of DNAs encompassed within the scope of the claim because SEQ ID NO: 2 may be combined with sequences known in the art,

e.g. expression vectors, the necessary common attribute is the ORF (SEQ ID NO: 2).

Weighing all factors including (1) that the full length ORF (SEQ ID NO: 2) is disclosed and (2) that any substantial variability within the genus arises due to addition of elements that are not part of the inventor's particular contribution, taken in view of the level of knowledge and skill in the art, one skilled in the art would recognize from the disclosure that the applicant was in possession of the genus of DNAs that comprise SEQ ID NO: 2.

Conclusion: The written description requirement is satisfied.

Example 9: Hybridization

Specification: The specification discloses a single cDNA (SEQ ID NO:1) which encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity. The specification includes an example wherein the complement of SEQ ID NO: 1 was used under highly stringent hybridization conditions (6XSSC and 65 degrees Celsius) for the isolation of nucleic acids that encode proteins that bind to dopamine receptor and stimulate adenylate cyclase activity. The hybridizing nucleic acids were not sequenced. They were expressed and several were shown to encode proteins that bind to a dopamine receptor and stimulate adenylate cyclase activity. These sequences may or may not be the same as SEQ ID NO: 1.

Claim:

An isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO: 1,

wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity.

Analysis:

A review of the full content of the specification indicates that the essential feature of the claimed invention is the isolated nucleic acid that hybridizes to SEQ ID NO: 1 under highly stringent conditions and encodes a protein with a specific function. The art indicates that hybridization techniques using a known DNA as a probe under highly stringent conditions were conventional in the art at the time of filing.

The claim is drawn to a genus of nucleic acids all of which must hybridize with SEQ ID NO: 1 and must encode a protein with a specific activity.

The search of the prior art indicates that SEQ ID NO: 1 is novel and unobvious.

There is a single species disclosed (a molecule consisting of SEQ ID NO: 1) that is within the scope of the claimed genus.

There is actual reduction to practice of the disclosed species.

Now turning to the genus analysis, a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of

skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.

Conclusion: The claimed invention is adequately described.

Example 14: Product by Function

Specification: The specification exemplifies a protein isolated from liver that catalyzes the reaction of A B. The isolated protein was sequenced and was determined to have the sequence as set forth in SEQ ID NO: 3. The specification also contemplates but does not exemplify variants of the protein wherein the variant can have any or all of the following: substitutions, deletions, insertions and additions. The specification indicates that procedures for making proteins with substitutions, deletions, insertions and additions is routine in the art and provides an assay for detecting the catalytic activity of the protein.

Claim:

A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A $\longrightarrow$ B.

Analysis:

A review of the full content of the specification indicates that a protein having SEQ ID NO: 3 or variants having 95% identity to SEQ ID NO: 3 and having catalytic activity are essential to the operation of the claimed invention. The procedures for making variants of SEQ ID NO: 3 are conventional in the art and an assay is described which will identify other proteins having the claimed catalytic activity. Moreover, procedures for making variants of SEQ ID NO: 3 which have 95% identity to SEQ ID NO: 3 and retain its activity are conventional in the art.

A review of the claim indicates that variants of SEQ ID NO: 3 include but are not limited to those variants of SEQ ID NO: 3 with substitutions, deletions, insertions and additions; but all variants must possess the specified catalytic activity and must have at least 95% identity to the SEQ ID NO: 3. Additionally, the claim is drawn to a protein which **comprises** SEQ ID NO: 3 or a variant thereof that has 95% identity to SEQ ID NO: 3. In other words, the protein claimed may be larger than SEQ ID NO: 3 or its variant with 95% identity to SEQ ID NO: 3. It should be noted that "having" is open language, equivalent to "comprising".

The claim has two different generic embodiments, the first being a protein which comprises SEQ ID NO: 3 and the second being variants of SEQ ID NO: 3. There is a single species disclosed, that species being SEQ ID NO: 3.

A search of the prior art indicates that SEQ ID NO: 3 is novel and unobvious.

There is actual reduction to practice of the single disclosed species. The specification indicates that the genus of proteins that must be variants of SEQ ID NO: 3 does not have substantial variation since all of the variants must possess the specified catalytic activity and must have at least 95% identity to the reference sequence, SEQ ID NO: 3. The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity. One of skill in the art would conclude that

applicant was in possession of the necessary common attributes possessed by the members of the genus.

Conclusion: The disclosure meets the requirements of 35 USC §112 first paragraph as providing adequate written description for the claimed invention.